DEC - 5 2011

Meridian Bioscience, Inc.	K112125: *illumigene*® Group B *Streptococcus* (GBS) DNA Amplification Assay	
	Description:	*illumigene*® GBS 510(k) Summary Statement
	Identification:	Attachment 002.002
	Date:	November 17, 2011

510(k) number: K112125 **Date of preparation:** November 17, 2011

Submitter: **Meridian Bioscience, Inc.**
Submitter's address: 3471 River Hills Drive
Cincinnati, Ohio 45244

Contact: Michelle Smith
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Device name: *illumigene*® Group B *Streptococcus* (GBS)
illumigene® Group B *Streptococcus* (GBS) External Control Kit

Common name: *Streptococcus* spp. Serological reagents
Classification name: Nucleic Acid Amplification Assay System, Group B Streptococcus Direct Specimen Test
NJR, CFR Section 866.3740

Predicate device: K062948: Cepheid® Smart GBS
Model SCGBS-100N-50

Reference comparator: Culture enrichment followed by bacterial culture with Group B *Streptococcus* identification

Description of the device:

The ***illumigene*** Molecular Diagnostic Test System is comprised of the ***illumigene***® Group B *Streptococcus* (GBS) DNA Amplification Test Kit, the ***illumigene*** Group B *Streptococcus* (GBS) External Control Kit and the ***illumipro-10*** Automated Isothermal Amplification and Detection System.

The ***illumigene*** Group B *Streptococcus* (GBS) DNA amplification assay utilizes loop-mediated isothermal amplification (LAMP) technology to detect the presence of *Streptococcus agalactiae* in enriched cultures obtained from vaginal/rectal swab specimens taken from antepartum women. Each ***illumigene*** GBS assay is completed using ***illumigene*** Control Reagent, ***illumigene*** Reaction Buffer, an ***illumigene*** GBS Test Device, and an ***illumigene*** Heat Treatment Tube. Samples are diluted with the ***illumigene*** Control Reagent, target DNA is made available for isothermal amplification via heat-treatment in the ***illumigene*** Heat Treatment Tube and DNA amplification occurs in the ***illumigene*** GBS Test Device.

The ***illumipro-10*** heats each ***illumigene*** GBS Test Device containing prepared samples and Control Reagent, facilitating amplification of target DNA. When *S. agalactiae* is present in the enriched culture sample, a conserved sequence of the *S. agalactiae* is amplified and magnesium pyrophosphate is formed. Magnesium pyrophosphate forms a precipitate in the reaction mixture. The ***illumipro-10*** detects the change in light transmission through the reaction mixture created by the precipitating magnesium pyrophosphate. Sample results are reported as Positive or Negative based on the detected change in light transmission.

The ***illumigene*** Group B *Streptococcus* (GBS) External Control Kit consists of a Positive Control Reagent and a Negative Control Reagent. External Control reagents are provided to aid the user in detection of reagent deterioration, adverse environmental or test conditions, or variance in operator performance that may lead to test errors. The ***illumigene*** Group B *Streptococcus* External Control Kit is required for routine Quality Control.

Intended Use:

The ***illumigene*** Group B *Streptococcus* (GBS) assay, performed on the ***illumipro-10***, is a qualitative *in vitro* diagnostic for the detection of *Streptococcus agalactiae* in enriched cultures obtained from vaginal/rectal swab specimens from antepartum women. Enriched cultures are obtained by 18-24 hour incubation of vaginal/rectal swab specimens in selective broth medium, either Lim Broth or TransVag Broth.

The ***illumigene*** GBS assay utilizes loop-mediated isothermal DNA amplification (LAMP)[1,2] technology to detect *Streptococcus agalactiae* by targeting a segment of the *Streptococcus agalactiae* genome. Results from the ***illumigene*** GBS assay can be used as an aid in establishing the GBS colonization status of antepartum women. This assay does not diagnose or monitor treatment for GBS infections. The ***illumigene*** GBS assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.

illumigene Group B *Streptococcus* is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

Comparison to predicate device:

Characteristic	*illumigene*® GBS	Cepheid® Smart GBS
Test Format	DNA Amplification Assay	DNA Amplification Assay
Intended Use		
DNA Amplification Technology	Loop-Mediated Isothermal Amplification (LAMP)	Real-Time Polymerase Chain Reaction (PCR)
Target Sequences Detected	213 base pair (bp) sequence residing in the 593-805 bp region of *S. agalactiae* genome Segment 3	Unique region of the *S. agalactiae* chromosome
Qualitative/Quantitative	Qualitative	Qualitative
Screening, Diagnostic or Identification Test	Diagnostic	Diagnostic
Specimen Types		
Vaginal/Rectal Swab Specimen	No	Yes (Direct Method)
Vaginal/Rectal Swab Specimen Enriched in Lim Broth	Yes	Yes (Enriched Method)
Vaginal/Rectal Swab Specimen Enriched in TransVag Broth	Yes	No
Reagents/Components	*illumigene* Control Reagent *illumigene* Reaction Buffer *illumigene* GBS Test Device *illumigene* Heat Treatment Tubes	Sample Preparation Reagent Treatment Reagent Lysis Reagent Master Mix Positive Control Negative Control

Characteristic	*illumigene*® GBS	Cepheid® Smart GBS
Extraction	Not applicable. Sample preparation by heat treatment. DNA extraction and purification not required.	Self-contained and automated
Amplification	Self-contained and automated	Self-contained and automated
Detection	Self-contained and automated	Self-contained and automated
Testing Time	Approximately 60 minutes	Approximately 75 minutes
Calibration	Not required	Not required
Controls		
Inhibition, Assay	Provided *illumigene* Control Reagent: Non-infectious Plasmid DNA, *S. aureus* insert *illumigene* GBS Test Device, Control Chamber: *Staphylococcus aureus* LAMP Primers	Provided Master Mix: Internal control DNA template Positive Control: Internal Control DNA template, non-infectious genomic GBS DNA Negative Control: Internal Control DNA template, non-infectious genomic DNA from *Streptococcus pneumoniae*
External	Adjunct Reagents *illumigene* Group B *Streptococcus* (GBS) External Control Kit, Catalog 279900	User Supplied KWIK-STIK Cepheid: Smart GBS QC Set from MicroBioLogics, catalog 8165; one each of *Streptococcus agalactiae* low- , moderate- and high-level positive control and *L. acidophilus* as negative control.
Extraction	Not Applicable Sample preparation, including heat treatment monitored by external thermometer and interval timer. Equipment is user supplied.	User Supplied
Equipment		
Instrumentation	*illumipro-10*™ Automated Isothermal Amplification and Detection System	SmartCycler® Dx System
General Laboratory Equipment	Micropipette 50 µL, 200 µL Dry-bath with 12 mm heat block, 95 C Digital Thermometer with Max/Min Temperature Memory Interval Timer Vortex Mixer	Vortex Mixer with microtube holder Microcentrifuge Micropipettors, 5 - 1000 µL range Cooling Block, 2 - 8 C Stopwatch or timer
Reading Method	Visible Light Transmission	Fluorescence

Characteristic	*illumigene*® GBS	Cepheid® Smart GBS
Results		
Group B Streptococcus Serotypes Tested	Ia, Ib, Ic, II, III, IV, V, VIa, VII, VIII, X	Ia/c, Ib/c, II, III. IV, IVc, V, VI, VII,VIII
Results Interpretation	INVALID POSITIVE NEGATIVE	POSITIVE NEGATIVE INVALID ND (Not Determined) NO RESULT
Performance		
Sensitivity	**97.4%** [95% CI: 91.9% - 99.0%]	**98.7%** [95% CI: 92.8% - 100.0%]
Specificity	**92.3%** [95% CI: 90.0% - 94.1%]	**90.4%** [95% CI: 85.8% - 93.9%]

Performance Comparison, Non-clinical Tests:

Interference Testing

Selected substances that might be expected to be present in vaginal/rectal swab samples taken from antepartum women were added to a negative Lim broth sample and two contrived positive Lim broth samples. The negative sample was prepared by pooling confirmed negative Lim Broth samples while the contrived positive samples were prepared by spiking a pooled, confirmed negative Lim sample with either *Streptococcus agalactiae*, strain 11248 Serotype Ia (123 CFU/test) or Streptococcus *agalactiae*, strain 12401 Serotype Ib (80 CFU/test). Potentially interfering substances were added to Lim broth samples at final concentrations of 2.5% v/v or greater when the substances could be pipetted. Substances that could not be pipetted were coated onto cotton swabs, immersed in the negative/positive Lim broth samples and tested. Dilution Controls were prepared by adding a phosphate buffered saline solution in place of the potentially cross-reactive organisms. Each inoculated sample was tested in triplicate.

The following substances, at the specified saturated solvent/diluents concentrations, do not interfere with ***illumigene*** Group B *Streptococcus* test results: Amniotic fluid (10% v/v), Human DNA (100 ng/Test), Urine (30%v/v), Whole Blood (2.5% v/v). The following substances do not interfere with test results: Meconium, Stool, Hemorrhoidal cream (30.65 mg/100mg), Miconazole (fungicide), Mucin (0.5-1.5%), Spermicidal gel (nonoxynol 9) (4 mg/100mg). Lubricating gel produced False Negative Results in 1 of 11 replicates tested. Body Powder produced False Negative Results in 1 of 10 replicates tested. Whole Blood at concentrations greater than 2.5% v/v interferes with the ***illumigene*** GBS assay.

Cross-reactivity Study

Potentially cross-reactive microorganisms expected to be present in vaginal/rectal swab specimens were added to negative and contrived positive Lim Broth samples. The negative sample was prepared by pooling confirmed negative Lim Broth samples. The contrived positive sample was prepared by spiking a confirmed negative matrix with Streptococcus *agalactiae*, strain 12401, at 122 CFU/test, near the limit of detection for this strain. Potentially cross-reactive microorganisms were added at concentrations of 1.2 x 10^8 CFU/mL (bacteria and fungi) or virus at a minimum of 1 x 10^5 $TCID_{50}$/mL (viruses). Dilution controls for each sample were prepared by adding sterile saline solution in place of the potentially cross-reactive microorganisms. Each sample was tested in triplicate. Cross-reactivity with *Enterococcus dispar* was observed in one of seven replicates tested.

The following microorganisms at the indicated concentrations do not interfere with ***illumigene*** GBS: *Aeromonas hydrophila, Alcaligenes faecalis, Bacillus cereus, Bacillus subtilis, Bacteroides fragilis, Campylobacter coli, Campylobacter fetus, Campylobacter jejuni, Candida albicans, Candida glabrata, Candida krusei, Candida parapsilosis, Candida tropicalis, Citrobacter freundii, Clostridium bifermentans, Clostridium butyricum, Clostridium difficile, Clostridium histolyticum, Clostridium novyi, Clostridium perfringens, Clostridium septicum, Clostridium sordellii, Clostridium sporogenes, Clostridium tetani, Corynebacterium genitalium, Corynebacterium urealyticum, Corynebacterium xerosis, Enterobacter aerogenes, Enterobacter cloacae, Enterococcus avium, Enterococcus durans, Enterococcus faecalis, Enterococcus faecium, Escherichia coli, Escherichia coli 0157:H7, Escherichia fergusonii, Escherichia hermannii, Gardnerella vaginalis, Haemophilus ducreyi, Helicobacter pylori, Klebsiella pneumoniae, Lactobacillus acidophilus, Lactobacillus brevis, Lactobacillus casei, Lactobacillus delbruekii subspecies lactis, Lactobacillus jensenii, Lactococcus lactis, Legionella pneumophila, Listeria monocytogenes, Moraxella osloensis, Morganella morganii, Neisseria gonorrhoeae, Peptostreptococcus anaerobius, Plesiomonas shigelloides, Porphyromonas asaccharolytica, Prevotella melaninogenica, Propionibacterium acnes, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Pseudomonus fluorescens, Salmonella Group B, Salmonella Group C, Salmonella Group D, Salmonella Group E, Serratia liquefaciens, Serratia marcescens, Shigella boydii, Shigella flexneri, Shigella sonnei, Staphylococcus aureus, Staphylococcus aureus (Cowan), Staphylococcus epidermidis, Staphylococcus saprophyticus, Streptococcus anginosus, Streptococcus bovis, Streptococcus dysgalactiae equisimilis, Streptococcus intermedius, Streptococcus mitis, Streptococcus oralis, Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus salivarius, Streptococcus sanguinis, Vibrio parahaemolyticus, Yersinia enterocolitica,* Adenovirus 40, Adenovirus 41, BK virus, Coxsackievirus, Echovirus, Epstein Barr virus, Herpes Simplex Virus-1, Herpes Simplex Virus-2, Rotavirus.

Mycoplasma genitalium, Mycoplasma hominis and Ureaplasma urealyticum were tested at final concentrations ranging between 1.6 x 10^6 and 9.9 x 10^6 CFU/mL with no reaction with the ***illumigene*** GBS assay.

Performance Comparison, Clinical Tests:

Clinical trials for the ***illumigene*** Group B *Streptococcus* (GBS) assay, including the ***illumipro-10*** Automated Isothermal amplification and detection system, were conducted in 2011. Performance characteristics of the ***illumigene*** GBS assay were determined by comparison to GBS bacterial culture. Four independent clinical test sites located in the Midwestern and Southern regions of the United States evaluated a total of 826 qualified patient samples. Samples were obtained according to established guidelines for the collection of clinical specimens for culture of Group B *Streptococcus* and enriched for 18-24 hours in either Lim Broth or TransVag Broth prior to ***illumigene*** testing. Four hundred three (403, 48.8%) specimens were enriched with Lim Broth and 423 (51.2%) specimens were enriched with TransVag Broth prior to testing. The age groups of patients tested ranged from 15 years of age to 44 years of age, with age unknown for 3 (0.4%) of the patient population. No differences in test performance were observed based on enrichment medium or patient age. Overall assay Sensitivity is reported as 97.4% [95% CI: 91.9% - 99.0%] where Specificity is 92.3% [95% CI: 90.0% - 94.1%]. Table 1 shows assay shows overall assay performance, including evaluation by enrichment medium; Table 2 summarizes assay performance by Clinical Site.

Table 1: Performance characteristics summary

Sample Type	Positive Samples			Negative Samples		
	illumigene/ Culture	% Sensitivity	95% CI	*illumigene*/ Culture	% Specificity	95% CI
Total	**150/154**	**97.4%**	**91.9 – 99.0%**	**610/661**	**92.3%**	**90.0 – 94.1%**
Lim	82/84	97.6%	91.7 - 99.3%	296/315	94.0%	90.8 – 96.1%
TransVag	68/70	97.1%	90.2 – 99.2%	314/346	90.8%	87.2 - 93.4%

Table 2: Performance characteristics summary

Site Identification	Enrichment Broth	Positive Samples			Negative Samples		
		illumigene /Culture	% Sensitivity	95% CI	*illumigene* /Culture	% Specificity	95% CI
Site 1	TransVag	32/33	97.0%	84.7 – 99.5%	197/199	99.0%	96.4 – 99.7%
Site 3	TransVag	36/37	97.3%	86.2 - 99.5%	117/147	79.6%	72.4 - 85.3%
Site 2	Lim	38/39	97.4%	86.8 - 99.5%	162/168	96.4%	92.4 – 98.4%
Site 4	Lim	44/45	97.8%	88.4 – 99.6%	134/147	97.8%	85.5 – 94.8%

Invalid results were obtained for 11/826 samples tested or 1.3%. Two of the 11 samples remained invalid after repeat testing of the original sample. Specimens that generated discrepant results were further evaluated by independent testing laboratories using FDA cleared or laboratory validated molecular assays. Sixteen of nineteen Lim Broth False Positive results were positive by an alternate molecular method. All thirty-two TransVag Broth False Positive results were positive by an alternate molecular method. In addition to discrepant sample analysis, a selection of concordant samples was tested with non-*illumigene* molecular methodologies. Concordant result testing showed a combined correlation between molecular methods of 97.7%.

Analytical Sensitivity

The analytical sensitivity of the *illumigene* Group B *Streptococcus* (GBS) assay was determined for six common *S. agalactiae* strains representing six serotypes. Analytical sensitivity is based on a minimum of 20 replicates for each measurand with a stated probability (eg, 95% where 19/20 replicates are positive) of obtaining positive responses. Analytical sensitivity testing is summarized below:

Serotype	*Streptococcus agalactiae* Strain Description	CFU/Test
Ia	NCTC 11248	60
Ib	ATCC 12401	80
Ic	NCTC 11253	640
II	II/2	320
III	ATCC 12403	160
V	ATCC BAA-611	1280

Additional *S. agalactiae* strains were tested and produced positive reactions at 1280 CFU/test with *illumigene* GBS. Strains and serotypes were tested as follows: **Serotype IV**: NCTC 11930; **Serotype VIa:** NCTC 08188; Serotype **VII:** VII/2; **Serotype VIII:** VIII/2; **Serotype X**: NCTC 11249; **Unknown Serotype:** ATCC 13813 and ATCC12386.

Reproducibility

Blind coded panels of 10 samples were supplied to three independent laboratories for reproducibility studies. Samples were randomly sorted within each panel to mask sample identities. The panels included contrived samples manufactured as low positive samples (i.e. limit of detection, n = 3) and high negative samples (n = 3). The panels also included contrived positive (n = 3) samples and natural negative samples (n = 1). Testing was performed by different operators at each site on the same day (intra-assay variability) for five days (inter-assay variability). Three lots of *illumigene* GBS and five *illumipro-10* instruments were used in this study. The results are given in the table below:

	Site 1		Site 2		Site 4		Total	
Sample Type	**Percent agreement**		**Percent agreement**		**Percent agreement**		**Percent agreement**	
Negative	10/10	100%	10/10	100%	10/10	100%	30/30	100%
High Negative	30/30	100%	30/30	100%	30/30	100%	90/90	100%
Low Positive	30/30	100%	30/30	100%	30/30	100%	90/90	100%
Positive	30/30	100%	30/30	100%	30/30	100%	90/90	100%

Conclusions

The ***illumigene*** Group B *Streptococcus* (GBS) assay, used in conjunction with the ***illumipro-10,*** can be used to detect *Streptococcus agalactiae* in vaginal/rectal specimens taken from antepartum women following culture enrichment in either Lim Broth or TransVag Broth. The test is diagnostic for Group B *Streptococcus*.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Meridian Bioscience, Inc.
c/o Susan D. Rolih
Director Quality Systems
3471 River Hills Drive
Cincinnati, OH 45244

DEC - 5 2011

Re: K112125
Trade/Device Name: *illumigene* ® Group B Streptococcus (GBS) DNA Amplification Assay
Regulation Number: 21 CFR § 866.3740
Regulation Name: Nucleic acid amplification assay system
Regulatory Class: Class I
Product Codes: NJR
Dated: November 17, 2011
Received: November 18, 2011

Dear Ms. Rolih:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

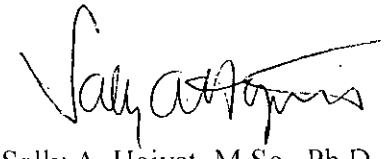
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice

requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,



Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Devices
Evaluation and Safety
Center for Devices and Radiological Health

Indication(s) for Use Form

510(k) Number (if known): K112125

Device Name: ***illumigene*** Group B *Streptococcus* (GBS) DNA Amplification Assay

Indications for Use:

The ***illumigene*** Group B *Streptococcus* (GBS) assay, performed on the ***illumipro-10™***, is a qualitative in vitro diagnostic for the detection of *Streptococcus agalactiae* in enriched cultures obtained from vaginal/rectal swab specimens from antepartum women. Enriched cultures are obtained by 18 - 24 hour incubation of vaginal/rectal swab specimens in selective broth medium, either Lim Broth [Todd Hewitt Broth supplemented with colistin (10 µg/mL) and nalidixic acid (15 µg/mL)] or TransVag Broth [Todd-Hewitt broth supplemented with gentamycin (8 µg/mL) and nalidixic acid (15 µg/mL)].

The ***illumigene*** GBS assay utilizes loop-mediated isothermal DNA amplification (LAMP) technology to detect *Streptococcus agalactiae* by targeting a segment of the *Streptococcus agalactiae* genome. Results from the ***illumigene*** GBS assay can be used as an aid in establishing the GBS colonization status of antepartum women. This assay is not intended to diagnose or monitor treatment for GBS infections.

The ***illumigene*** GBS assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.

illumigene Group B *Streptococcus* is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

Prescription Use ___X____ Over-The-Counter Use _____

(Part 21 CFR 801 Subpart D) AND/OR (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K112125